Diabetes Prevention Program Background

- **Type 2 diabetes is the major cause of premature mortality and morbidity due to cardiovascular, renal, ophthalmic and neuological diseases.**
- **People at risk for developing type 2 diabetes have a high incidence of cardiovascular disease.**
- **The Diabetes Prevention Program (DPP) is:**
  - **a randomized, clinical trial conducted in 27 U.S. centers**
  - **designed to test whether preventing or delaying type 2 diabetes may prevent its complications**

The Diabetes Prevention Program Research Group. *Diabetes Care* 1999;22:623-634

Diabetes Prevention Program

Purpose

Compare the effects of the insulin sensitizers, metformin and troglitazone*, to placebo or intensive lifestyle intervention on the progression to type 2 diabetes in a high-risk population having:

- **impaired glucose tolerance (IGT) *and* elevated fasting glucose**
- **≥ 50% women**
- **about 20% age 65 years or older**
- **about 50% ethnic minority: African-American, Hispanic, American Indian, Asian American**

***Discontinued in June, 1998**

The Diabetes Prevention Program Research Group. *Diabetes Care* 1999;22:623-634

Diabetes Prevention Program Study Objectives

Primary objectives

Compare safety and efficacy of 3 interventions for preventing or delaying development of diabetes

- **Standard lifestyle recommendations + masked metformin titrated to 850 mg BID**
- **Standard lifestyle recommendations + masked placebo**
- **Intensive lifestyle intervention by case managers with the goals of:**
  - **≥ 7% weight reduction through healthy eating and physical activity**
  - **≥ 150 min/week moderate intensity physical activity**

The Diabetes Prevention Program Research Group. *Diabetes Care* 1999;22:623-634

Diabetes Prevention Program Study Objectives

Secondary objectives

Assess effects of interventions on:

- **Cardiovascular disease and its risk factors**
- **Changes in glycemia, b-cell function, insulin sensitivity, body composition, physical activity, nutrient intake, and health-related QOL**
- **Adverse events**

The Diabetes Prevention Program Research Group. *Diabetes Care* 1999;22:623-634

Diabetes Prevention Program Study Design

Inclusion Criteria

- Age ≥ 25 years
- BMI ≥ 24 kg/m^2 (≥ 22 kg/m^2 for Asian Americans)
- IGT (2 hour glucose 140-199 mg/dL after 75 g OGTT)
- Elevated FPG (95-125 mg/dL) except in American Indians

Exclusion Criteria

- Diagnosed diabetes at baseline, except GDM
- Medical conditions that increase the risk of early mortality or medical intervention
- Medications, medical conditions and/or behaviors that may interfere with the conduct of the trial

The Diabetes Prevention Program Research Group. *Diabetes Care* 1999;22:623-634

Diabetes Prevention Program Lifestyle Interventions

Standard lifestyle interventions

- All randomized participants received written information and 20 - 30 minute session with case manager to encourage:
  - a healthy diet
  - loss of 5 - 10% of initial weight
  - gradual increase in activity (*eg,* walking) ≥ 30 minutes 5 days/week
  - avoidance of excessive alcohol intake
  - smoking cessation
- Annual review of recommendations

The Diabetes Prevention Program Research Group. *Diabetes Care* 1999;22:623-634

Diabetes Prevention Program Lifestyle Interventions

Intensive lifestyle interventions

- Frequent sessions with a case manager, including:
  - ≥ 16 sessions during the first 24 weeks
    - Instruction in diet, exercise and behavior modification
    - Encouragement to achieve and maintain weight-loss goals by fat reduction, then calorie reduction
  - At least monthly contact thereafter
- Two optional, supervised exercise sessions per week
- "Tool box" strategies as needed to achieve goals
- 4-6 week group courses offered quarterly

The Diabetes Prevention Program Research Group. *Diabetes Care* 1999;22:623-634

Diabetes Prevention Program Diabetes Assessment

- Tests for diabetes included annual OGTT, semiannual FPG and FPG whenever symptoms were present
- Diabetes was diagnosed if FPG $\geq$ 126 mg/dL or OGTT 2-h plasma glucose $\geq$ 200 mg/dL was confirmed by 2 tests
- Diabetes diagnosis was revealed to participants, DPP investigators and primary care providers
  - If FPG <140 mg/dL, coded treatment was continued if acceptable to the participant and physician
  - If FPG $\geq$ 140 mg/dL, the patient discontinued coded medication and was referred for diabetes care.
- Scheduled visits continued to collect outcomes data.

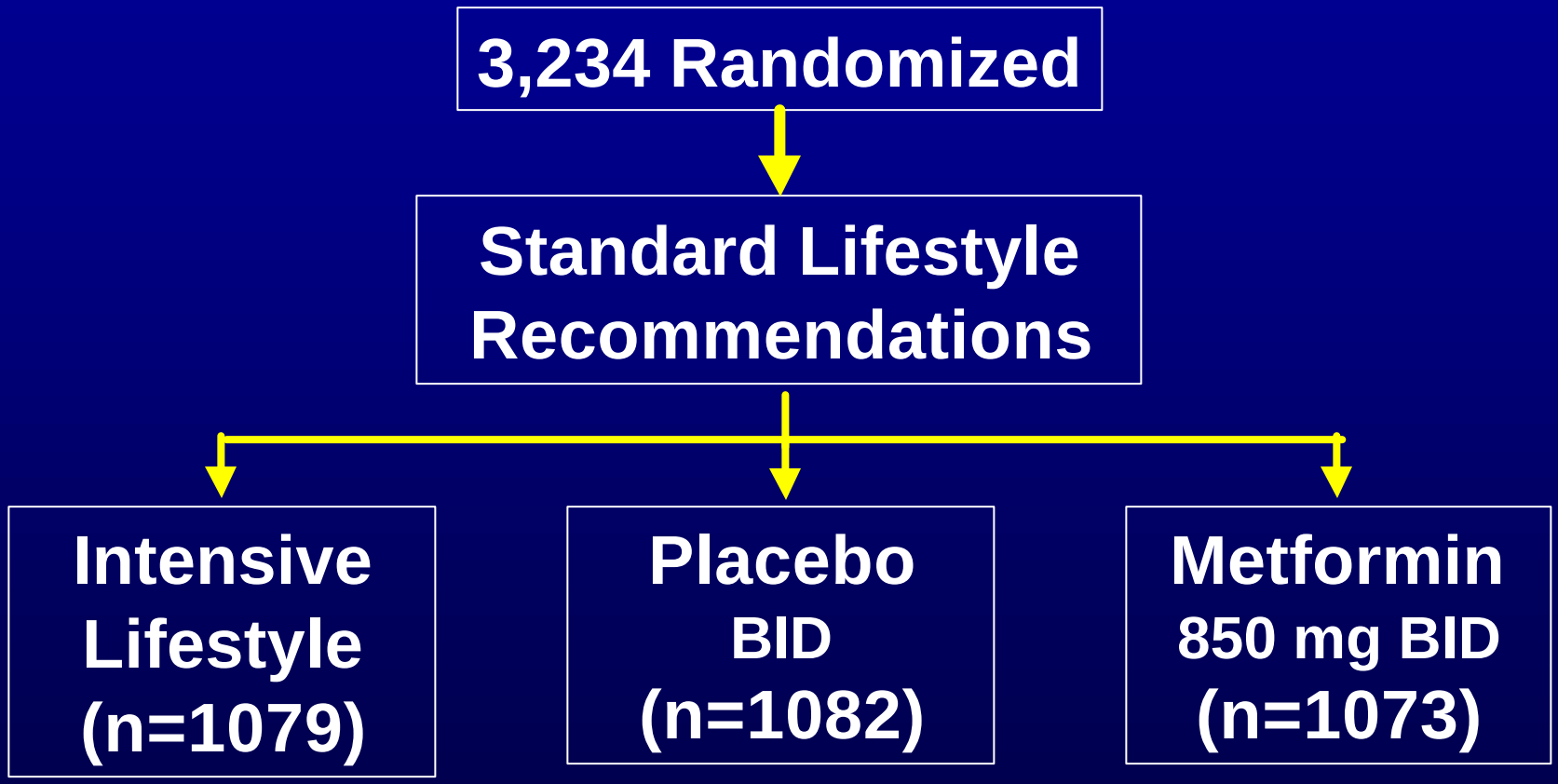
The Diabetes Prevention Program Research Group. *Diabetes Care* 1999;22:623-634

Diabetes Prevention Program Time and Event Line

June 1996	**Recruitment began**
June 1998	**Discontinued troglitazone arm**
Spring 1999	**Recruitment completed**
May 2001	**Early discontinuation of double-blind treatment because of efficacy provided by both interventions**

The Diabetes Prevention Program Research Group. *Diabetes Care* 1999;22:623-634

Diabetes Prevention Program Randomization Scheme



The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

Diabetes Prevention Program Baseline Demographics

	Placebo	Metformin	Intensive Lifestyle
Age (years)	50.3	50.9	50.6
Gender (M/F)	31%/ 69%	34%/ 66%	32%/ 68%
Ethnicity			
Caucasian	54%	56%	54%
African-American	20%	21%	19%
Hispanic	16%	15%	17%
American Indian	6%	5%	6%
Asian American*	5%	3%	5%

*** Includes 20 Pacific Islanders**

The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

Diabetes Prevention Program Baseline Patient Characteristics

	Placebo	Metformin	Intensive Lifestyle
Family History of Diabetes	70%	68%	70%
History of GDM (women)	16%	16%	16%
Leisure Activity (met-hr/week)	17	16	17
Waist/Hip Ratio	0.9	0.9	0.9
Waist (cm)	105	105	105
BMI (kg/m^2)	34.2	33.9	33.9

The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

Diabetes Prevention Program Baseline Glycemic Measurements

	Placebo	Metformin	Intensive Lifestyle
FPG (mg/dL)	107	107	106
2-h OGTT (mg/dL)	165	165	164
HbA_{1c} (%)	5.9	5.9	5.9

The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

Diabetes Prevention Program
Achievement of Study Goals

Average follow-up of 2.8 years

Lifestyle Modifications	Goal	% Achieving Goal Week 24	% Achieving Goal Last Vist
Weight loss	≥ 7%	50%	38%
Physical activity (min/week)	≥ 150	74%	58%

Pharmacological Intervention		Placebo	Metformin
Compliance	≥ 80%	77%	72%
Full dose	2 tablets/day	97%	84%

The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

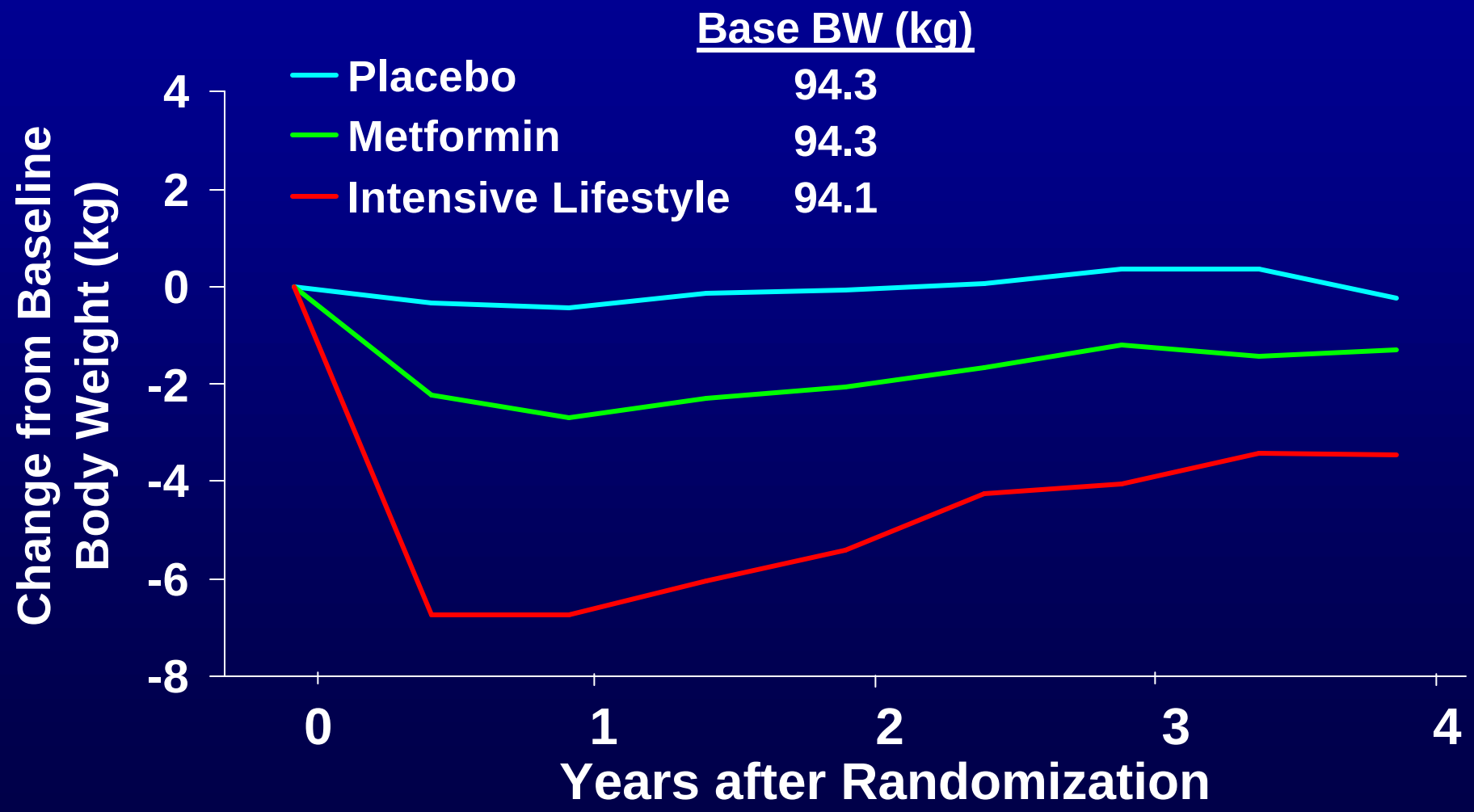
Diabetes Prevention Program
Effects on Weight and Dietary Intake

	Placebo	Metformin	Lifestyle Intervention	P
Change in Weight (kg)	-0.1	-2.1	-5.6	<0.001
Change in Fat Intake* (% of total calories)	-0.8%	-0.8%	-6.6%	<0.001
Change in Energy Intake (kcal/day) at 1 yr	-249	-296	-450	<0.001

*Baseline fat intake was 34.1% of total calories. The goal of intensive lifestyle modification was < 25% of total calories.

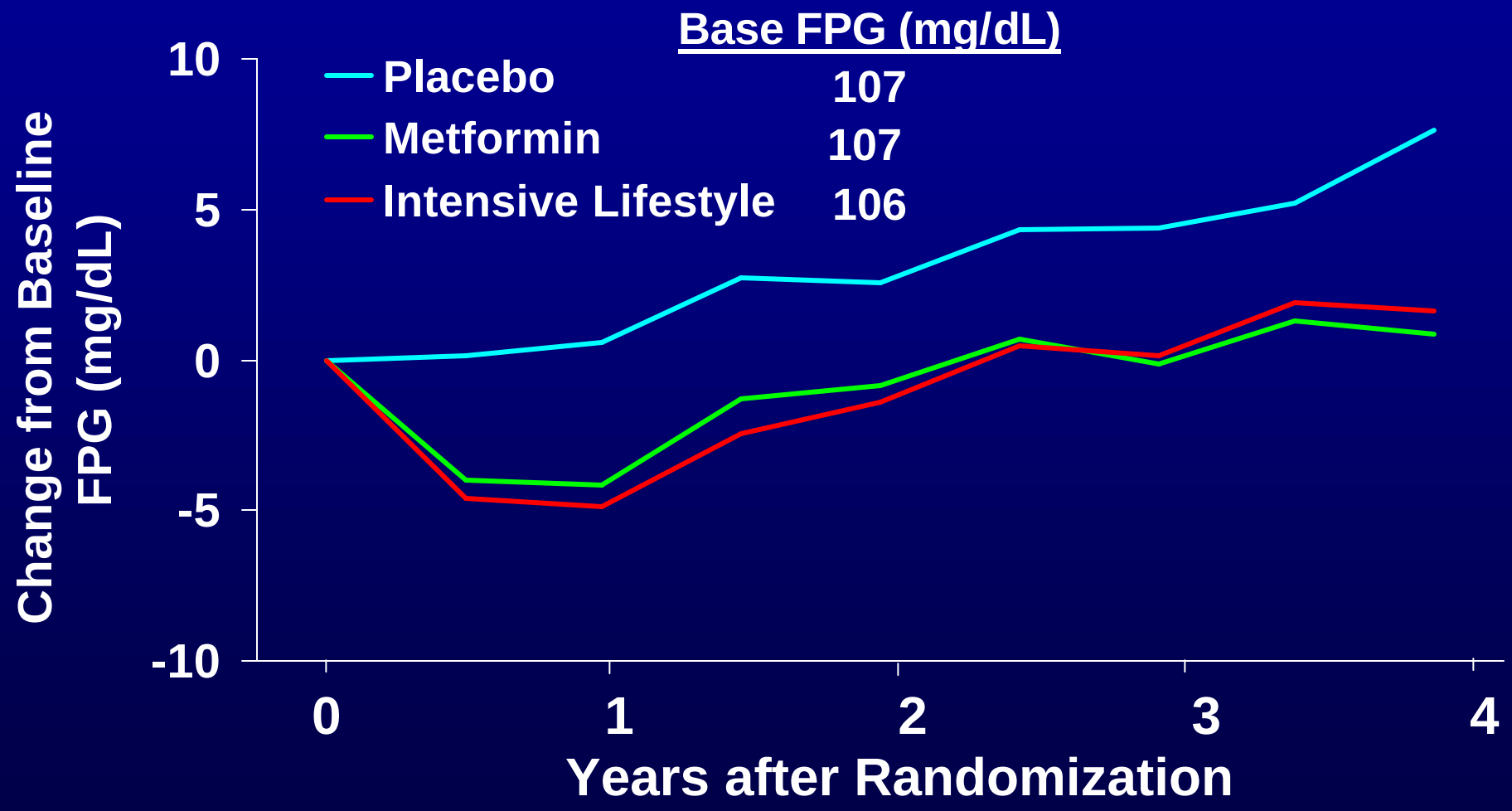
The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

Diabetes Prevention Program
Change in Body Weight



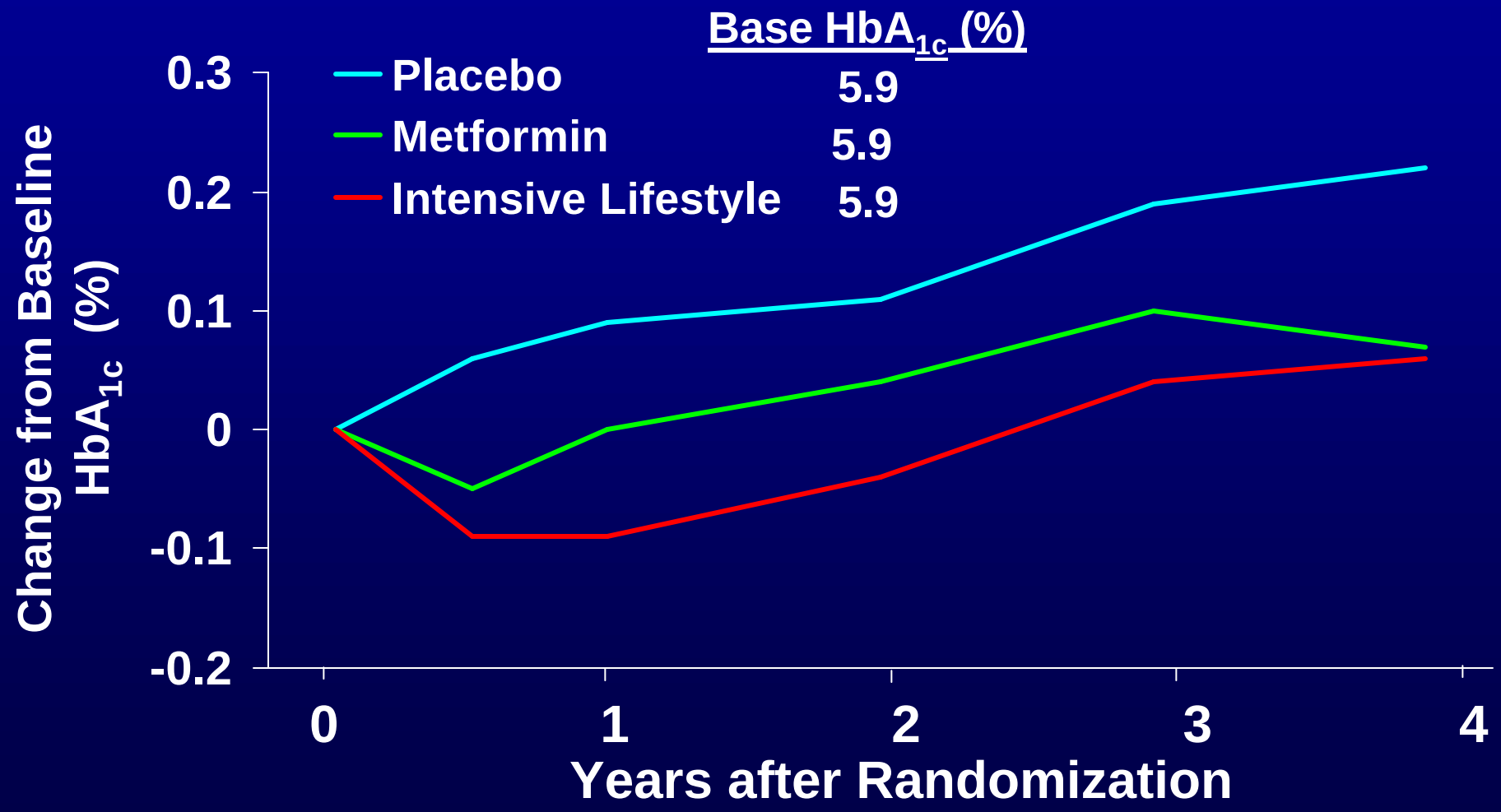
The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

Diabetes Prevention Program
Change in Fasting Plasma Glucose



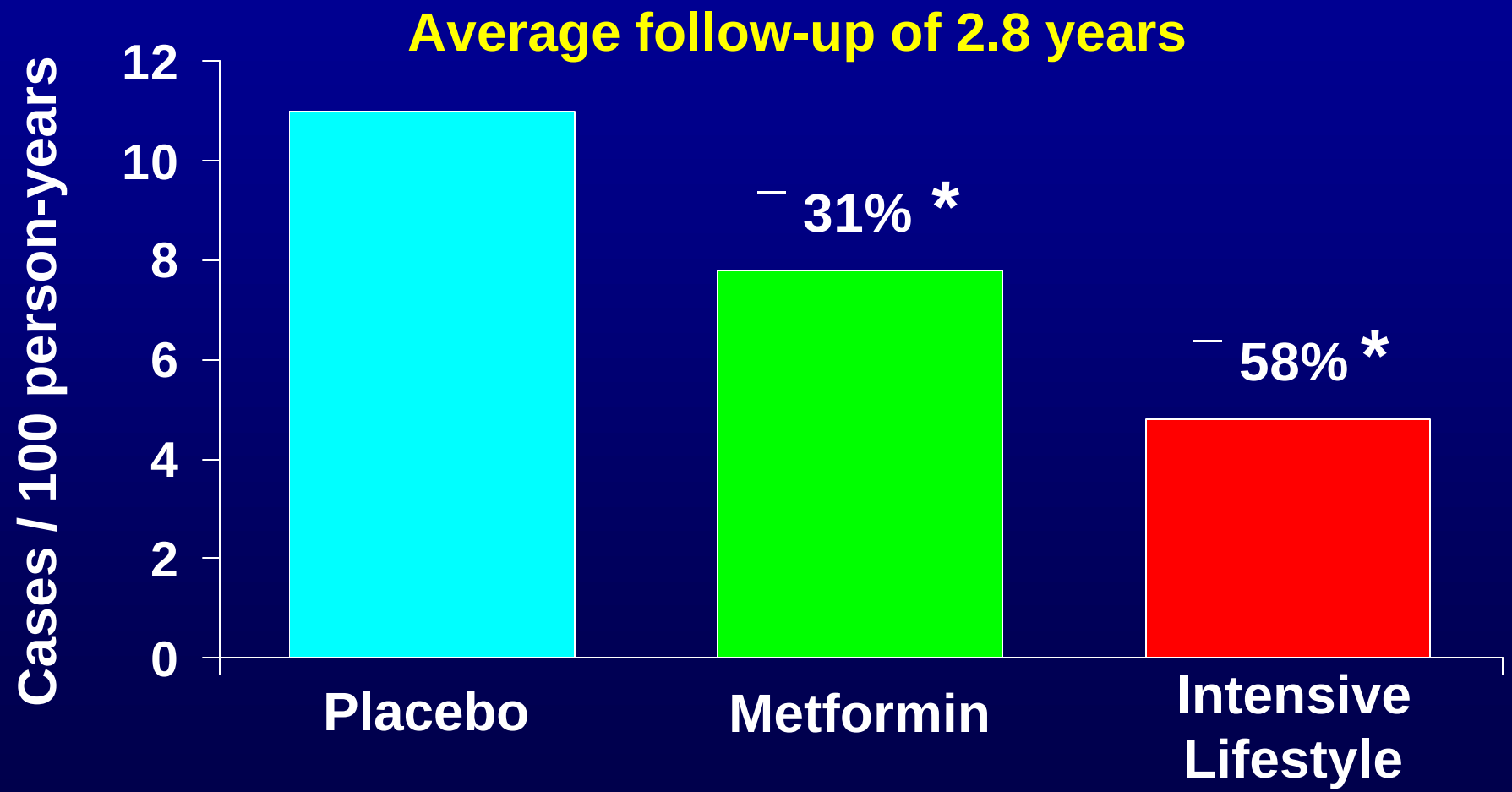
The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

Diabetes Prevention Program
Change in HbA_{1c}



The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

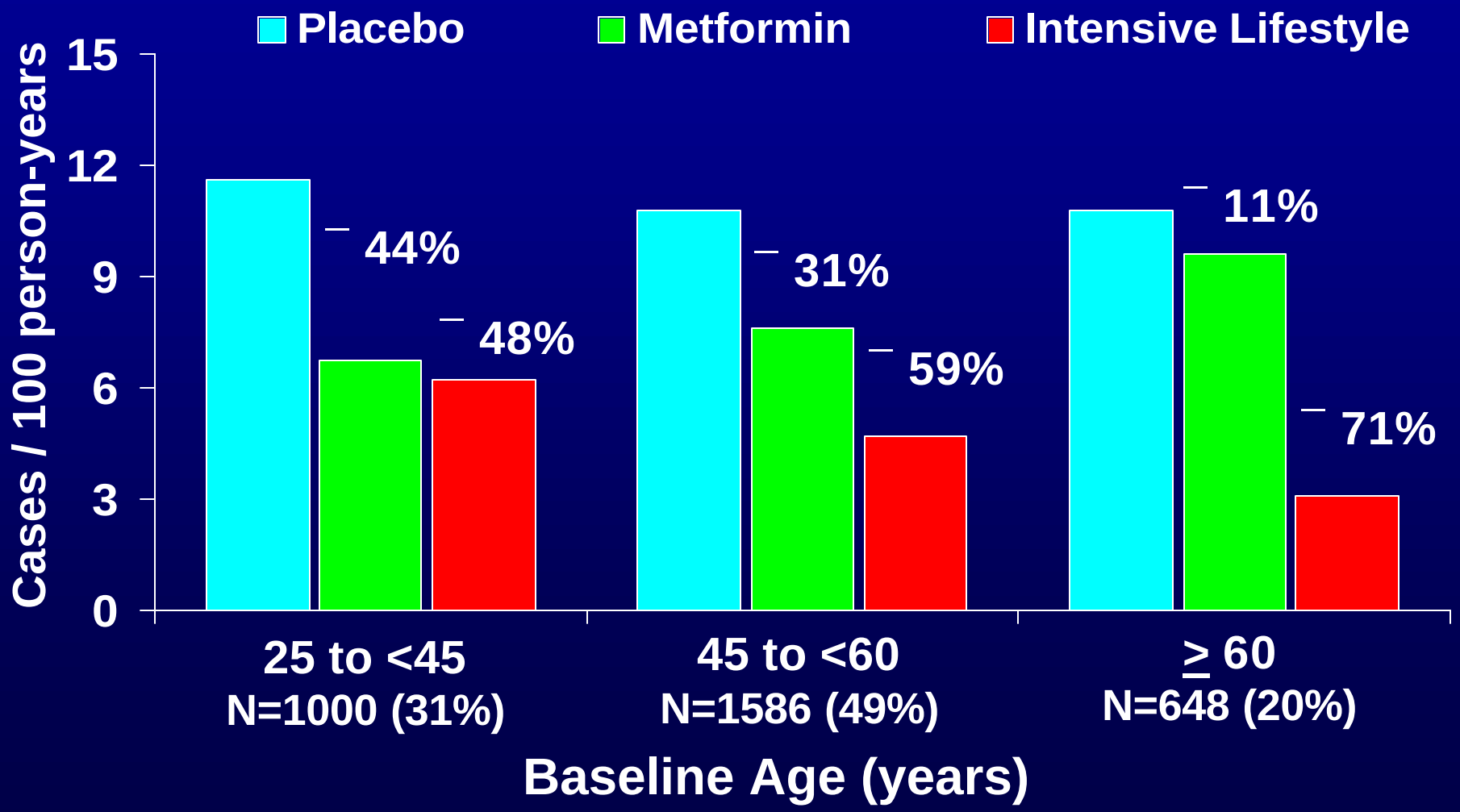
Diabetes Prevention Program
Progression to Type 2 Diabetes



***All pair-wise comparisons significantly different by group sequential log-rank test**

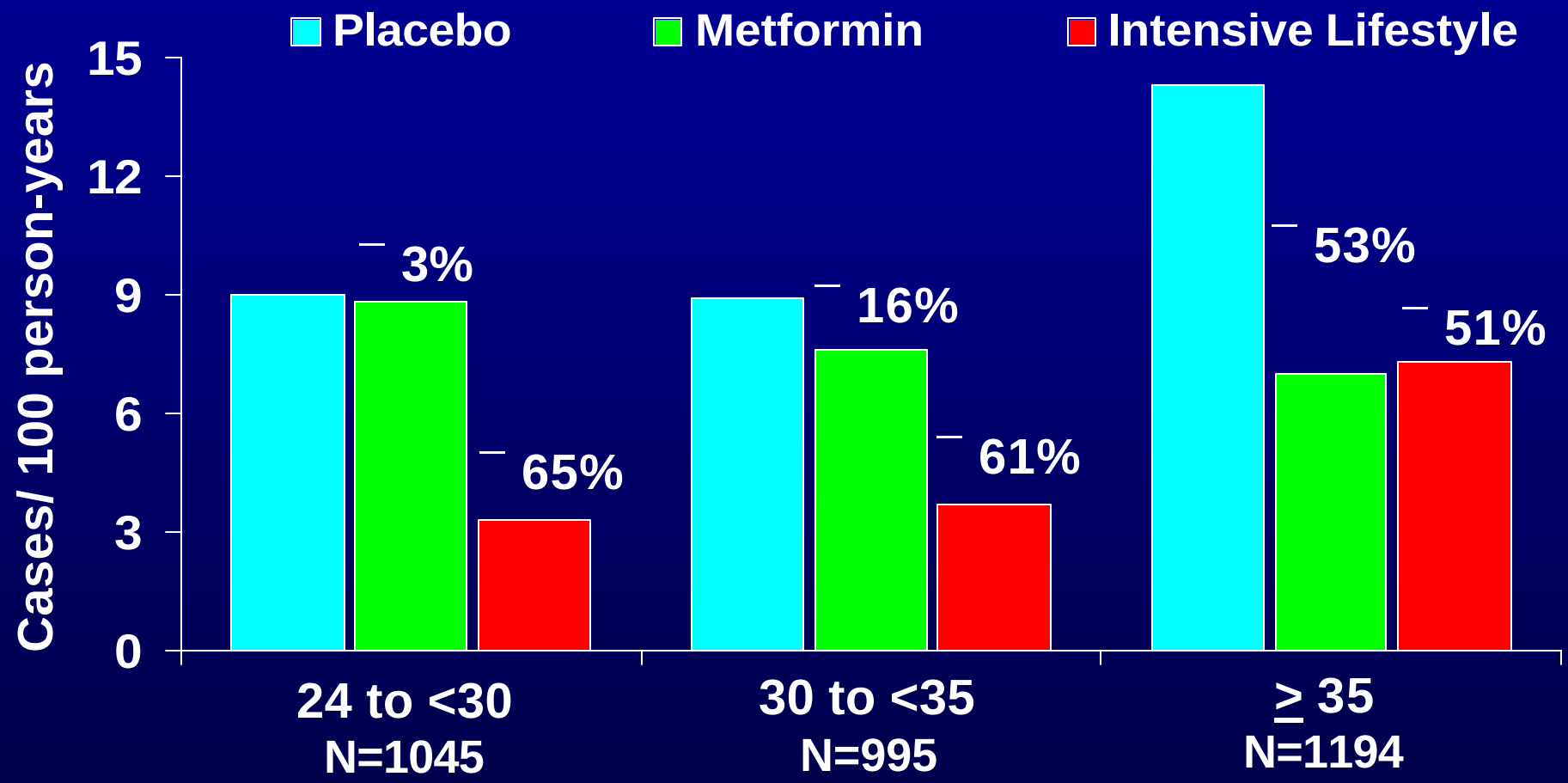
The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

Diabetes Prevention Program
Progression to Type 2 Diabetes by Age



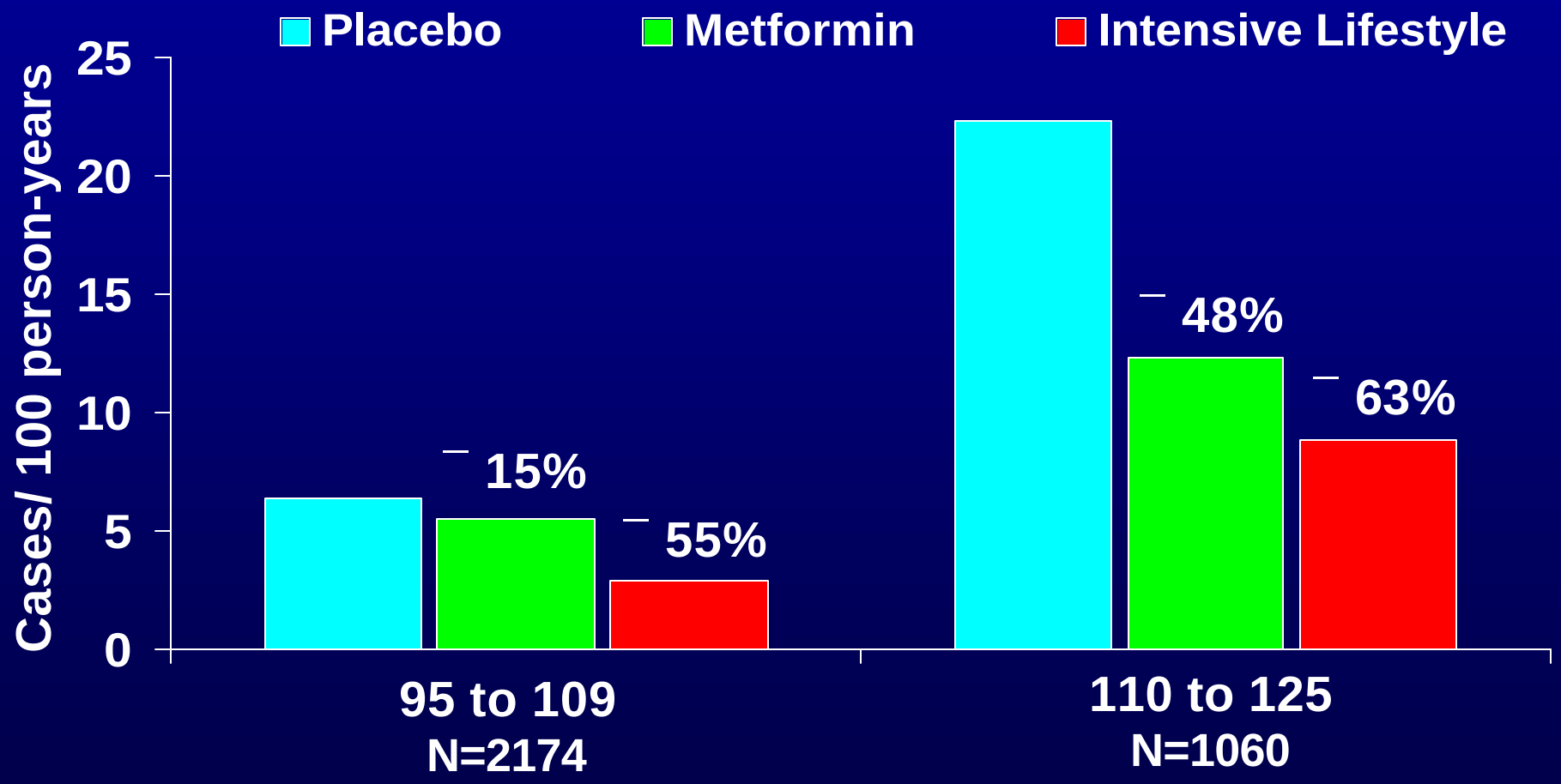
The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

Diabetes Prevention Program
Progression to Type 2 Diabetes by BMI



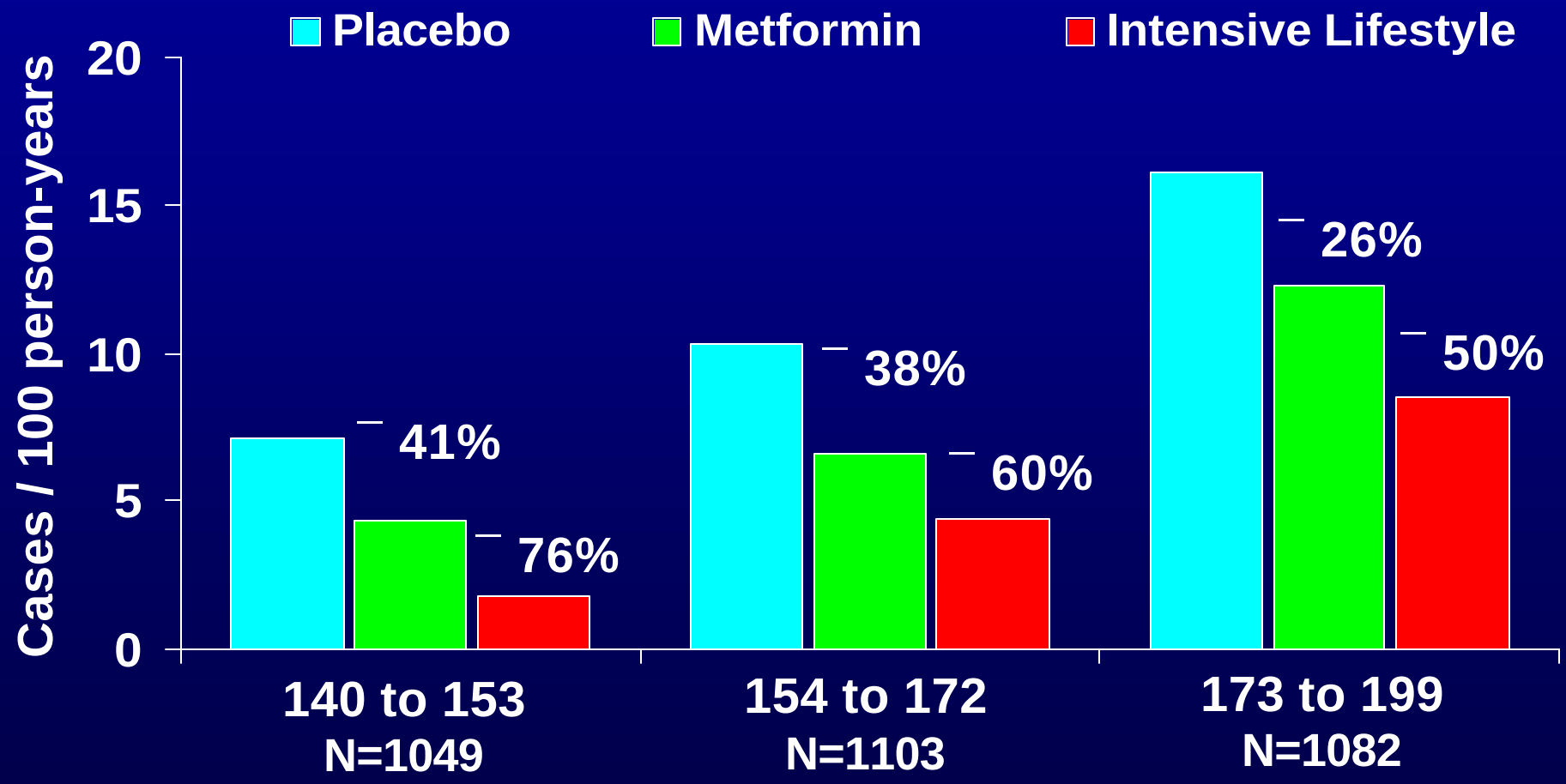
The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

Diabetes Prevention Program
Progression to Type 2 Diabetes by FPG



The Diabetes Prevention Program Research Group. *New Engl J Med* 2002; 346:393-403.

Diabetes Prevention Program
Progression to Type 2 Diabetes by 2-hr PG



The Diabetes Prevention Program Research Group. *New Engl J Med* 2002;346:393-403.

Conclusions

- **Intensive lifestyle modifications and metformin each reduced the risk of developing type 2 diabetes among a high-risk population of persons with IGT.**
- **Lifestyle modification was most effective for individuals 60 and older and for those with lower baseline BMI.**
- **Metformin reduced the risk of developing type 2 diabetes most effectively in the DPP participants younger than 60 years and those with a baseline BMI >35 kg/m^2.**